Systemic Response to Microgravity: Utilizing GeneLab datasets to identify molecular targets for future hypotheses-driven spaceflight studies

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Biological risks associated with microgravity are a major concern for long-term space travel. Although determination of risk has been a focus for NASA research, data examining systemic (i.e., multi- or pan-tissue) responses to space flight are sparse. To perform our analysis, we utilized the NASA GeneLab database which is a publicly available repository containing a wide array of “omics” results from experiments conducted with: i) with different flight conditions (space shuttle (STS) missions vs. International Space Station (ISS); ii) a variety of tissues; and 3) assays that measure epigenetic, transcriptional, and protein expression changes. Meta-analysis of the transcriptomic data from 7 different murine and rat data sets, examining tissues such as liver, kidney, adrenal gland, thymus, mammary gland, skin, and skeletal muscle (soleus, extensor digitorum longus, tibialis anterior, quadriceps, and gastrocnemius) revealed for the first time, the existence of potential “master regulators” coordinating systemic responses to microgravity in rodents. We identified p53, TGFβ1 and immune related pathways as the highly prevalent pan-tissue signaling pathways that are affected by microgravity responses. Some variability in the degree of change in their expression across species, strain and time of flight was also observed. Interestingly, while certain skeletal muscle (gastrocnemius and soleus) exhibited an overall down-regulation of these genes, some other muscle types such as the extensor digitorum longus, tibialis anterior and quadriceps, showed an up-regulated expression, indicative of potential compensatory mechanisms to prevent microgravity-induced atrophy. Key genes isolated by unbiased systems analyses displayed a major overlap between tissue types and flight conditions and established TGFβ1 to be the most connected gene across all data sets. Finally, a set of microgravity responsive miRNA signature was identified and based on their predicted functional state and subsequent impact on health, a theoretical “health risk score” was calculated. The genes and miRNAs identified from our analyses can be targeted for future research involving efficient countermeasure design. Our study thus exemplifies the utility of GeneLab data repository to aid in the process of performing novel hypothesis – based spaceflight research aimed at elucidating the global impact of environmental stressors at multiple biological scales.